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               S L1

     FILE 'REGISTRY' ENTERED AT 14:49:54 ON 27 SEP 2005
L2           1 S L1 FULL

     FILE 'CAPLUS' ENTERED AT 14:49:54 ON 27 SEP 2005
L3           2 S L2 FULL

     FILE 'REGISTRY' ENTERED AT 14:52:20 ON 27 SEP 2005
L4             STRUCTURE UPLOADED

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               S L5

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L6           0 S L5 SSS FULL

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L9           0 S L8 FULL
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               S L10

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     FILE 'CAPLUS' ENTERED AT 14:58:49 ON 27 SEP 2005
L12          0 S L11 SSS FULL
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               S L13

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L15          3 S L14
               S L13

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L16         17 S L13 FULL

     FILE 'CAPLUS' ENTERED AT 15:01:40 ON 27 SEP 2005
L17       1295 S L16 FULL
L18         13 S L17 AND (CYAN? OR NITRILE)
L19          1 S L18 AND REDUC?
L20          7 S L18 AND HYDRO?
L21          0 S L20 AND BASE
L22          2 S L20 AND PY<2001
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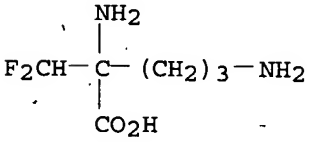
L22 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:466216 CAPLUS
DOCUMENT NUMBER: 109:66216
TITLE: Validity of short-term examination for antipromoters of bladder carcinogenesis
AUTHOR(S): Kakizoe, Tadao; Takai, Kazuhiro; Tobisu, Kenichi; Ohtani, Mikinobu; Sato, Shigeaki
CORPORATE SOURCE: Urol. Div., Natl. Cancer Cent. Hosp., Tokyo, 104, Japan
SOURCE: Japanese Journal of Cancer Research (**1988**), 79(2), 231-5
CODEN: JJCREP; ISSN: 0910-5050
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Various compds. were screened for antipromoter activity in bladder carcinogenesis in rats with a view to using them clin. to inhibit postoperative intravesical ectopic tumor growth of superficial papillary bladder cancer. Their inhibitions of the effect of Na saccharin in maintaining increased agglutinability of bladder cells by Con A were examined in 4-wk tests. The compds. found to inhibit the effect of saccharin were α-tocopherol, ascorbic acid, aspirin, all-trans aromatic retinoid, α-difluoromethylornithine, sodium **cyanate** and p,p'-diaminodiphenylmethane. Considering the toxicities of some of these chems., ascorbic acid and α-difluoromethylornithine were concluded to be the most promising for future clin. trials.

IT **70052-12-9**, α-Difluoromethylornithine
RL: PRP (Properties)
(antipromoter effects of, on bladder carcinogenesis)
RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



L22 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:146047 CAPLUS
DOCUMENT NUMBER: 108:146047
TITLE: Putrescine derivatives as substrates of spermidine synthase
AUTHOR(S): Sarhan, S.; Dezeure, F.; Seiler, N.
CORPORATE SOURCE: Merrell Dow Res. Inst., Strasbourg, 67084, Fr.
SOURCE: International Journal of Biochemistry (**1987**), 19(11), 1037-47
CODEN: IJBOBV; ISSN: 0020-711X
DOCUMENT TYPE: Journal
LANGUAGE: English

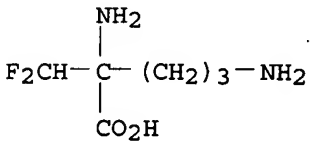
AB Derivs. of 1,4-butanediamine (putrescine) were studied in vitro and in vivo as potential substrates of spermidine synthase. Substituents in the 1-position decreased the reaction rate by steric hindrance, and in the case of electron-withdrawing groups there was an addition decrease due to the lowered basicity of the vicinal amino group. Substituents in the 2-position were tolerated; under saturating conditions, reaction rates were comparable to those of putrescine. Compds. which were identified as substrates of spermidine synthase in vitro formed derivs. of spermidine and spermine in vivo. However, compds. such as 1-methylputrescine formed in vivo only a spermidine derivative, because the 2nd aminopropylation was sterically hindered by the substituent on the C atom next to the amino group. The administration of 2-**hydroxyputrescine** to α-difluoromethylornithine-pretreated chick embryos produced spermidine and spermine analogs in amts. exceeding spermidine and spermine formation from putrescine under comparable conditions. Since the concentration of 2-**hydroxyputrescine** in the embryo was higher than that of

putrescine and all other putrescine analogs, uptake of the polyamine precursor from the yolk may be rate-limiting. Three days after administration of 5 mM α-difluoromethylornithine, there was a near-to-complete arrest of embryonal growth. A series of diamines supported growth under these conditions, even if they were not substrates of spermidine synthase. The survival of chick embryos was, however, only supported if the diamines were capable of forming significant amts. of spermidine and spermine analogs.

IT **70052-12-9**, DL-α-Difluoromethylornithine
RL: BIOL (Biological study)
(chick embryo response to, putrescine analogs effect on)

RN 70052-12-9 CAPLUS

CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



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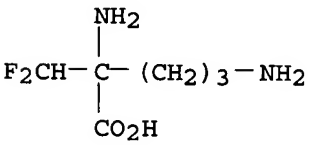
L19 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:98548 CAPLUS
DOCUMENT NUMBER: 126:207158
TITLE: A cytotoxicity assay for evaluation of candidate anti-Pneumocystis carinii agents
AUTHOR(S): Cushion, Melanie T.; Chen, Franklin; Kloepfer, Natalie
CORPORATE SOURCE: Dep. Internal Med., Univ. Cincinnati Coll. Med., Cincinnati, OH, 45627-0560, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1997), 41(2), 379-384
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of over 60 agents representing several different classes of compds. were evaluated for their effects on the ATP pools of Pneumocystis carinii populations derived from immunosuppressed rats. A cytotoxicity assay based on an ATP-driven bioluminescent reaction was used to determine the concentration of agent which decreased the P. carinii ATP pools by 50% vs. untreated controls (IC50). A ranking system based on the IC50 values was devised for comparison of relative responses among the compds. evaluated in the cytotoxic assay and for comparison to in vivo efficacy. With few exceptions, there was a strong correlation between results from the ATP assay and the performance of the compound in vivo. Antibiotics, with the exception of trimethoprim-sulfamethoxazole (TMP-SMX), were ineffective at **reducing** the ATP pools and were not active, clin. or in the rat model of P. carinii pneumonia. Likewise, other agents not expected to be effective, e.g., antiviral compds., did not show activity. Standard anti-P. carinii compds., e.g., TMP-SMX, pentamidine, and dapsone, dramatically **reduced** ATP levels. Analogs of the quinone and topoisomerase inhibitor groups were shown to **reduce** ATP concns. and hold promise for further in vivo investigation. The cytotoxicity assay provides a rapid assessment of response, does not rely on replicating organisms, and should be useful for assessment of structure-function relationships.

IT **70052-12-9**, DFMO
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytotoxicity assay for evaluation of candidate anti-Pneumocystis carinii agents)

RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 STRUCTURE UPLOADED

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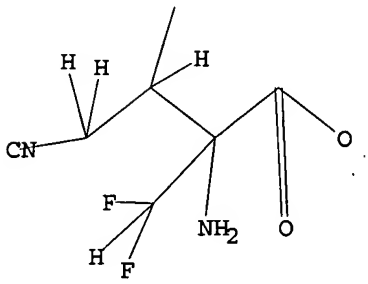
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

FULL SEARCH INITIATED 14:49:54 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 314 TO ITERATE

100.0% PROCESSED 314 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

L2 1 SEA SSS FUL L1

L3 2 L2

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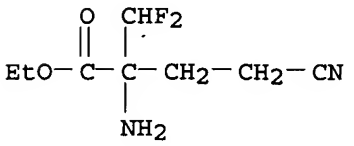
L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:263671 CAPLUS
DOCUMENT NUMBER: 142:463986
TITLE: Catalytic hydrogenation of ethyl 2-amino-2-difluoromethyl-4-cyanobutanoate and its Schiff base reaction modes
AUTHOR(S): Zhu, Jingyang; Price, Benjamin A.; Walker, Jonathan; Zhao, Shannon X.
CORPORATE SOURCE: Process Research & Development, Bristol-Myers Squibb Company, New Brunswick, NJ, 08903, USA
SOURCE: Tetrahedron Letters (2005), 46(16), 2795-2797
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Under heterogeneous catalysis, 2-amino-2-[di(fluoro)methyl]-4-(cyano)butanoic acid Et ester or its Schiff base could be selectively reduced in good yield by hydrogenation to give a diamine, or to form a five-membered ring or a six-membered ring heterocycles. This selectivity is highly dependent on the type of catalysts used. The hydrogenation of 2-amino-4-cyano-2-[di(fluoro)methyl]butanoic acid Et ester gave 2-[di(fluoro)methyl]ornithine Et ester dihydrochloride. The hydrogenation of a Schiff base derivative, 4-cyano-2-[di(fluoro)methyl]-2-[[di(phenyl)methylene]amino]butanoic acid Et ester using Raney cobalt gave

3-amino-3-[di(fluoro)methyl]-2-piperidinone.

IT **501011-46-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(study of hydrogenation of (amino)(cyano)[di(fluoro)methyl]butanoic acid ester using com. catalysts and differing reaction conditions)

RN 501011-46-7 CAPLUS

CN Butanoic acid, 2-amino-4-cyano-2-(difluoromethyl)-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:202415 CAPLUS
DOCUMENT NUMBER: 138:221839
TITLE: Processes for the production of α-difluoromethyl ornithine (DFMO)
INVENTOR(S): Zhu, Jingyang; Chadwick, Scott T.; Price, Benjamin A.; Zhao, Shannon X.; Costello, Carrie A.; Vemishetti, Purushotham
PATENT ASSIGNEE(S): Women First Healthcare, Inc., USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003020209	A2	20030313	WO 2002-US26990	20020823
WO 2003020209	A3	20040304		
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US 6730809	B2	20040504		
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EP 1421058	A2	20040526	EP 2002-768695	20020823
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BR 2002012153	A	20040713	BR 2002-12153	20020823
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US 2004171876	A1	20040902	US 2004-788728	20040226

PRIORITY APPLN. INFO.:

US 2001-315832P	P	20010829
US 2002-224890	A1	20020819
WO 2002-US26990	W	20020823

OTHER SOURCE(S): CASREACT 138:221839; MARPAT 138:221839

AB Processes and synthetic intermediates for the preparation of H2NCH2CH2CH2C(CHF2)(NH2)CO2H (DFMO) are described. Thus, condensation of glycine Et ester hydrochloride with benzaldehyde (MgSO4/Et3N/MeCN), addition reaction with acrylonitrile (K2CO3/Et3N+CH2Ph Cl-), reaction with ClCHF2 (LiOBu-t/THF), and deprotection (4 N HCl/MTBE) yielded

NCCH2CH2C(CHF2)(NH2)CO2H. Hydrogenolysis over 10% Pd/C in MTBE and treatment with 12 N HCl afforded DFMO.HCl (.apprx. 75 % pure by 1H NMR).

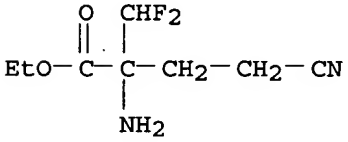
IT **501011-46-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(production of α-difluoromethyl ornithine)

RN 501011-46-7 CAPLUS

CN Butanoic acid, 2-amino-4-cyano-2-(difluoromethyl)-, ethyl ester (9CI) (CA INDEX NAME)



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